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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No.	:	09/994,495	Confirmation No.:	1098
Applicants	:	Ralph SOMACK et al.		
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Examiner	:	William H. BEISNER		
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BRIEF FOR APPELLANTS

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Sir:

This appeal is from the decision of the Primary Examiner dated February 7, 2005, finally rejecting claims 1-19, 48, and 49, which are reproduced as an Appendix to this brief.

A Notice of Appeal and the Notice of Appeal fee of $500.00, were filed on May 9, 2005. The fee for filing an appeal brief of $500.00 pursuant to 37 C.F.R. § 41.20(b)(2), along with two (2) extra copies of this brief, are being filed herewith, along with a Petition for a One-Month Extension of TimeThe Commissioner is hereby authorized to charge any appropriate fees under 37 C.F.R. §§ 1.16, 1.17, and 1.21, that may be required by this paper, and to credit any overpayment, to Deposit Account No. 50-0925.

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I. Real Party in Interest

The present application is assigned to Applera Corporation as evidenced by the Assignment recorded January 30, 2002, at Reel 012584, Frames 0020-0024, and the Assignment recorded on January 14, 2003 at Reel 013367, Frames 0173-0183.

II. Related Appeals and Interferences

Neither Appellants' legal representative, nor Assignee, knows of any other appeal or interference which will affect, or be directly affected by, or have bearing on, the Board's decision in the present pending appeal.

III. Status of Claims

Claims 1-49 and 51-57 are pending in this application. Claims 20-47 and 51-57 have been withdrawn from consideration as drawn to a non-elected invention. The final rejection of claims 1-19, 48, and 49, is hereby appealed.

IV. Status of Amendments

No amendments have been filed after the final rejection of claims 1-19, 48, and 49, dated February 7, 2005.

V. Summary of Invention

(a) Independent Claim 1

Finally rejected independent claim 1 is directed to a system 40 for processing a plurality of fluid samples (*see,* for example, paragraph [0072]). The system comprises a plurality of biological sample purification devices 8 comprising a tubular body 10 having a first end 11, a first end opening 14, a second end 21, and second end opening 18, a species-immobilizing filter 20 held within the tubular body 10, and a removable cap 16 to seal the second end opening 18 (*see,* Fig. 1); and a sealing device having a surface adapted to individually seal each of the first end openings 14 of the plurality of devices 8 during the processing of a plurality of fluid samples, the sealing device

comprising a tray 24 and the tray 24 comprising a plurality of recesses 42. *See*, for example, paragraphs [0008], [0011], [0036], and [0067]-[0073], and Fig. 1.

(b) Dependent Claim 2

Dependent claim 2 depends from independent claim 1, and therefore includes all of the features of claim 1, as discussed above. Moreover, claim 2 is directed to the system wherein the plurality of recesses 42 are formed in the surface of the sealing device, the sealing device is adapted to receive the first ends 11 of the plurality of devices 8 in respective ones of the recesses 42, and the sealing device is adapted to seal the first end openings 14 of the plurality of devices 8 when the respective first ends 11 of the plurality of devices 8 are received in the recesses 42 (*see,* paragraphs [0067]-[0073], and Fig. 1).

(c) Dependent Claim 3

Dependent claim 3 depends from independent claim 1, and therefore includes all of the features of claim 1, as discussed above. Moreover, claim 3 is directed to the system wherein each device 8 of the plurality of devices 8 further includes a second removable cap 12 adapted to seal the first end opening 14 of the respective device 8 (*see,* for example, paragraphs [0006] and [0067], and Fig. 1).

(d) Dependent Claim 4

Dependent claim 4 depends from dependent claim 3, and therefore includes all of the features of claims 1 and 3, as discussed above. Moreover, claim 4 is directed to the system wherein at least one device 8 of the plurality of devices 8 has the respective removable cap 16 attached to the second end 21 of the device 8 and the respective second removable cap 12 attached to the first end 11 of the device 8 (*see*, paragraphs [0006] and [0067], and Fig. 1).

(e) Dependent Claim 5

Dependent claim 5 depends from dependent claim 3, and therefore includes all of the features of claims 1 and 3, as discussed above. Moreover, claim 5 is directed to the system wherein each device 8 of said plurality of devices 8 includes the respective removable cap 16 attached to the second end 21 of the device 8 and the respective removable cap 12 attached to the first end 11 of the device 8 (*see,* for example, paragraphs [0006] and [0067], and Fig. 1).

(f) Dependent Claim 6

Dependent claim 6 depends from independent claim 1, and therefore includes all of the features of claim 1, as discussed above. Moreover, claim 6 is directed to the system wherein the species-immobilizing filter 20 of each device 8 is positioned within the tubular body 10 of the respective device 8 such that the ratio of (1) the distance from the filter 20 to the first end 11, (2) the distance from the filter 20 to the second end 21, is greater than or equal to about 4:1 (*see,* for example, paragraphs [0033] and [0034] and Fig. 1).

(g) Dependent Claim 7

Dependent claim 7 depends from independent claim 1, and therefore includes all of the features of claim 1, as discussed above. Moreover, claim 7 is directed to the system wherein the species-immobilizing filter 20 of each device 8 is positioned at the second end 21 of the respective tubular body 10 (*see*, for example, paragraph [0034] and Fig. 1).

(h) Dependent Claim 8

Dependent claim 8 depends from independent claim 1, and therefore includes all of the features of claim 1, as discussed above. Moreover, claim 8 is directed to the system wherein the first end opening 14 of each device 8 of the plurality of devices 8 is sealed with the sealing device, and the sealing device includes an adhesive (*see,* for example, paragraphs [0031] and [0072]).

(i) Dependent Claim 9

Dependent claim 9 depends from dependent claim 8, and therefore includes all of the features of claims 1 and 8, as discussed above. Moreover, claim 8 is directed to the system wherein the adhesive is optically-curable, pressure sensitive, or both (*see,* for example, paragraphs [0036] and [0072]).

(j) Dependent Claim 10

Dependent claim 10 depends from independent claim 1, and therefore includes all of the features of claim 1, as discussed above. Moreover, claim 10 is directed to the system wherein the species-immobilizing filter 20 of each device 8 comprises a nucleic acid purification membrane (*see,* for example, paragraph [0037]).

(k) Dependent Claim 11

Dependent claim 11 depends from independent claim 1, and therefore includes all of the features of claim 1, as discussed above. Moreover, claim 11 is directed to the system further including a target analyte bound to the species-immobilizing filter 20 of at least one device 8 of the plurality of devices 8, the target analyte comprising a nucleic acid or nucleic acid fragment (*see,* for example, paragraphs [0007] and [0079]).

(l) Dependent Claim 12

Dependent claim 12 depends from dependent claim 11, and therefore includes all of the features of claims 1 and 11, as discussed above. Moreover, claim 12 is directed to the system wherein the at least one device 8 that includes the target analyte also contains a polymerase chain reaction solution, a transcription solution, a reverse transcription solution, or a reverse transcription polymerase chain reaction solution (*see,* for example, paragraphs [0078] at lines 3-5, and [0079] at lines 1-5).

(m) Dependent Claim 13

Dependent claim 13 depends from independent claim 1, and therefore includes all of the features of claim 1, as discussed above. Moreover, claim 13 is directed to the system further including a biological sample that comprises an animal cell lysate or a plant cell lysate, within the tubular body 10 of at least one device 8 of the plurality of devices 8 (*see*, for example, paragraph [0049] at lines 3-6).

(n) Dependent Claim 14

Dependent claim 14 depends from independent claim 1, and therefore includes all of the features of claim 1, as discussed above. Moreover, claim 14 is directed to the system further including a biological sample that comprises whole blood, within the tubular body 10 of at least one device 8 of the plurality of devices (*see*, for example, paragraphs [0047] at lines 1-2 and paragraph [0049] at lines 1-2).

(o) Dependent Claim 15

Dependent claim 15 depends from independent claim 1, and therefore includes all of the features of claim 1, as discussed above. Moreover, claim 15 is directed to the system further including a biological sample that comprises tissue extract, within the tubular body 10 of at least one device 8 of the plurality of devices 8 (*see*, for example, paragraph [0049] at lines 3-6).

(p) Dependent Claim 16

Claim 16 is directed to a purification apparatus including the system of claim 1, and therefore includes all of the features of claim 1, as discussed above. Moreover, claim 16 is directed to a purification apparatus wherein the first end opening 14 of each device 8 of the plurality of devices 8 is sealed by the sealing device in the form of an assembly (*see*, for example, paragraph [0073]).

(q) Dependent Claim 17

Dependent claim 17 depends from dependent claim 16, and therefore includes all of the features of claims 1 and 16, as discussed above. Moreover, claim 17 is directed to the purification apparatus wherein the assembly further comprises a second sealing device, the second sealing device having a surface adapted to seal the second end openings 18 of the plurality of devices 8 (*see*, for example, paragraphs [0008] at lines 6-8, [0011] at lines 17-20, and [0036] at lines 6-10, and Figs. 5 and 6).

(r) Dependent Claim 18

Dependent claim 18 depends from dependent claim 17, and therefore includes all of the features of claims 1, 16, and 17, as discussed above. Moreover, claim 18 is directed to a purification apparatus wherein the surface of the second sealing device has a plurality of recesses therein, the second sealing device is adapted to received the second ends 21 of two or more of the devices 8 in respective ones of the recesses, and the second sealing device is adapted to seal the second end openings 18 of the plurality of devices 8 when the respective second ends 21 of the devices 8 are received in the recesses (*see,* for example, paragraphs [0006] at lines 18-20, [0011] at lines 18-21, [0030] at lines 5-11, [0031], [0036] at lines 1-10, and sealing tray 24 illustrated in Fig. 5).

(s) Dependent Claim 19

Dependent claim 19 is directed to a purification apparatus and includes the system of claim 2, and therefore includes all of the features of claims 1 and 2, as discussed above. Moreover, claim 19 is directed to a purification apparatus wherein each device 8 of the plurality of devices 8 is positioned with the respective first end 11 thereof received within a corresponding one of the recesses in the sealing device, in the form of an assembly (*see*, for example, paragraphs [0030] at lines 1-11 and [0031]).

(t) Independent Claim 48

Independent claim 48 is directed to an analytical system 50 for manipulating biological samples, comprising a plate 58 having a first surface 60 and a second surface 62 that opposes the first surface 60, and a plurality of through-holes 52, each through-hole 52 extending from the first surface 60 to the second surface 62 and defining a first end opening 64 at the first surface 60 and a second end opening 65 at the second surface 62 (*see*, paragraphs [0008] and [0051], and Figs. 7 and 8); a plurality of species-immobilizing filters 54 (*see*, paragraph [0008] and Figs. 7 and 8), each disposed within a respective one of the through-holes 52; and a first sealing device having a surface adapted to individually seal each first end opening 64 of the plurality of through holes 52 during the manipulation of biological samples, the first sealing device comprising a tray and the tray comprising a plurality of recesses (*see*, Figs. 7, 8, and 11); and a second sealing device adapted to

seal each second end opening 65 of the plurality of through-holes 52 (*see*, for example, Figs. 7, 8, and 11, and paragraph [0051] which describes that the tubular device and array tray can be replaced with a plate system that can include sealing trays, removable caps, where additional components mentioned with reference to other embodiments are suitable in the plate system configuration, Fig. 5, paragraphs [0008], [0017], [0030], and [0031]).

(u) Dependent Claim 49

Dependent claim 49 depends from independent claim 48, and therefore includes all of the features of claim 48, as discussed above. Moreover, claim 49 is directed to the system wherein the second sealing device comprises a plurality of removable end caps adapted to individually seal the second end openings 65 of the plurality of through-holes 52 (*see*, for example, paragraphs [0051] and [0008] at lines 7-8).

VI. The Issues

(a) Whether claims 1-5, 16, and 19 are anticipated under 35 U.S.C. § 102(b) by U.S. Patent No. 5,603,899 to *Franciskovich et al.*

(b) Whether claims 1-9 and 16-19 are unpatentable under 35 U.S.C. § 103(a) as being unpatentable over *Franciskovich et al.* in view of U.S. Patent No. 5,342,581 to *Sanadi.*

(c) Whether claims 10, 11, and 13-15 are unpatentable under 35 U.S.C. § 103(a) over *Franciskovich et al.* in view of U.S. Patent No. 5,846,493 to *Bankier et al.*

(d) Whether claim 12 is unpatentable under 35 U.S.C. § 103(a) over *Franciskovich et al.* in view of *Bankier et al.* taken further in view of U.S. Patent No. 5,955,271 to *Leying et al.* and U.S. Patent No. 5,124,041 to *Sheer et al.*

(e) Whether claims 48 and 49 are unpatentable under 35 U.S.C. § 103(a) over U.S. Patent No. 5,151,719 to *Fernwood et al.* in view of *Sanadi.*

(f) Whether claims 48 and 49 are unpatentable under 35 U.S.C. § 103(a) over U.S. Patent No. 5,368,823 to *McGraw et al* in view of *Sanadi.*

VII. Grouping of Claims

Claims 1-7 and 10-17 stand or fall together. Claims 8 and 9 stand or fall together. Claims 48-49 stand or fall together. Appellants explain below why claims 1 and 8, are separately patentable.

VIII. Argument

(a) Claims 1-5, 16, and 19 are novel in view of *Franciskovich et al.*

Claims 1-5, 16, and 19 have been rejected under 35 U.S.C. § 102(b) as being anticipated by *Franciskovich et al.*

35 U.S.C. § 102(b) states:

> "...the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of the application for patent in the United States...."

In an Examiner Interview held on November 5, 2004, the Examiner agreed that *Franciskovich et al.* '899 did not teach that plate member 36 sealed each of the openings 70 of the two members in view of the fact that the vacuum is simultaneously applied to all ends.

In the Final Office Action, the Examiner asserts while the foregoing was agreed to, it was later found that *Franciskovich et al.* disclosed an embodiment where a centrifuge is used to drive the sample through the tube. In that embodiment, '899 teaches that the gasket 15 need not be provided between the column manifold 14 and the collector plate 16 having a plurality of recesses where a recess corresponds to a respective end of a tube provided in the column manifold, such that the skirt-like flange 28 on the column manifold 14 fits into a recess 44 around the upper surface 36 of the collector plate 16. The Examiner asserts that this engagement meets the present limitation in claims 1-5, 16, and 19 of "... a sealing device having a surface adapted to individually seal each of the first end openings of said plurality of devices..., the sealing device comprising a tray and the tray comprising a plurality of recesses." The Examiner states that "... the tray seals the first end openings during processing of the fluid samples. The tray is sealed to plate (14) holding the devices (12) during centrifugation.... Vacuum port (80) and gasket (15) are not required and/or used in the centrifugal processing...."

It is submitted that *Franciskovich et al.* does not teach a collector plate 16 having an upper surface 36 that ***seals*** each of openings 70 of the plurality of devices 12 held in manifold 14, let alone a collector plate 16 having an upper surface 36 that ***individually seals*** each of the openings 70 of the plurality of devices 12 held in manifold 14. Accordingly, it is submitted that collector plate 16 having upper surface 36, does not meet the present limitation of having a "surface adapted to individually seal of each of the first end openings...."

Present claim 1 requires a sealing device having a surface adapted to "***individually seal***" each of the first end openings of the plurality of devices, and the sealing device comprises a tray and the tray comprises a plurality of recesses.

Applicants are entitled to rely upon the plain meaning of the term "individually seal" recited in the subject claims. The term "seal" is both implicitly and explicitly defined in the present specification and is an art-recognized term. *See* the present specification at paragraph [0012], lines 5-6, which describes that a sealed device 8 is sealed such that a sample sealed therein is protected such that it does not evaporate or leak from the device, and is not subject to contamination. Paragraph [0073] implicitly defines the term "seal" as being a seal sufficient to maintain, for example, one or more agents, reagents, or other components, ***in*** the sealed device when the sealed device is , for example, subjected to thermo-cycling as required for PCR, transcription, RT, RTPCR, or another process. In further support of the foregoing, the term "seal" is an art recognized term and is defined, for example, in the "Terminology Reference System" of the U.S. Environmental Protection Agency as "seal (technical)...any device or system that creates a non-leaking union between two mechanical or process-system elements...." Applicants note that the Federal Circuit in *SeaChange Int'l., Inc. v. C-Cor Inc.*, No.: 04-1375-1498 (Fed. Cir. 2005), used a technical dictionary, i.e., "The New IEEE Standard Dictionary of Electrical and Electronics Terms, 842 (5th ed. 1993)," to aid in construing the claim term "network."

(i) It is submitted that *Franciskovich et al.* fails to teach a sealing device having a surface adapted to "***individually seal***" each of the first end openings of the plurality of devices, and the sealing device comprises a tray and the tray comprises a plurality of recesses. *Franciskovich et al.* fails to teach individually sealing each of openings 70 with collector plate 16; and

(ii) It is further submitted that *Franciskovich et al.* teaches away from the claimed invention by suggesting that a seal is ***not*** provided between the column manifold 14 and the collector plate 16 when a centrifuge is employed to drive the sample.

Franciskovich et al. describes a processing apparatus 10 that includes a plurality of separation columns 12 held within a column manifold 14 which rests on a collector plate 16. *See,* column 2, lines 53-56 and Fig. 1. *See*, Figs. 1 and 4. The cross-sectional area of the cylindrical well portion 38 of the collector plate 16 is significantly greater than the cross-sectional area of the aperture 24 and therefore greater than each opening 70 of each separation column 12, which diameter difference aids in gathering material expelled from the associated separation column 12 and concentrating that material in the bottom region of the respective well 34 of the collector plate 16. *See, Franciskovich et al.* at column 3 at lines 20-21 and lines 27-33. *Franciskovich et al.* further describes at column 3 at lines 34-40, that the column manifold 14 is assembled on the collector plate 16, and that an annular skirt-like flange 28 on the column manifold 14 fits into the recess 44 around the upper surface 36 of the collector plate 16, and that this engagement of the flange 28 within the recess 44 "***limits***" horizontal movement of the column manifold 14 and maintains each of the apertures 24 aligned over a separate well 34 in the collector plate 16. *Franciskovich et al.* ***never*** teaches that a seal is provided between collector plate 16 and each opening 70, and further ***never*** teaches that column manifold 14 in contact with collector plate 16, forms a "seal." Rather, *Franciskovich et al.* states that the column manifold 14 ***"rests"*** on top of the collector plate 16, or is "assembled" onto the collector plate 16, or that the engagement of the flange 28 of column manifold 14 within the recess 44 of collector plate 16 "limits horizontal movement" of the column manifold 14, and maintains alignment.

In the Final Office Action dated February 7, 2005, the Examiner asserts that the passage in *Franciskovich et al.* at column 4, lines 60 to column 5, line 20, and column 5, line 59 to column 6, line 4, establishes that *Franciskovich et al.* teaches individually sealing each opening 70. Again, the Examiner states that a centrifuge is used rather than vacuum, and that gasket 15 is not required to communicate port 80 with the openings and that in the absence of gasket 15, the openings are sealed by the plate 16 as is required in the instant claims.

Again, *Franciskovich et al.* does not teach or suggest individually sealing openings 70 using collector plate 16. Instead, *Franciskovich et al.*, at column 4, lines 60-63, states:

> "After all of the separation columns **12** have been inserted, the column manifold **14** is placed on top of the collection plate **16** with the truncated corners **46** and **48** of the components aligned to ensure proper fit of the components."

This passage recites simply that the manifold is "placed" on top of the collector plate such that the components are "aligned" and does ***not*** teach or suggest that end opening 70 are individually sealed.

In further support of the foregoing, *Franciskovich et al.* teaches at column 5, lines 9-15 that during the centrifuging process, a sample that has been placed in the upper portion of the separation column 12 is driven through the separation medium which entraps selected material in the sample, and that other constituents of the sample ***pass out the opening*** 70 in the end tube 62 and into well 34 in collector plate 16. This passage of *Franciskovich et al.* clearly communicates that openings 70 are ***not*** sealed, since a sample passes through the opening 70 when manifold 14 is disposed on collector plate 16.

As discussed above, the Examiner also points to column 5, line 59 to column 6, line 4, as teaching that each individual opening 70 is sealed. Column 5, lines 59-63, states:

> "The column manifold 14 is then placed on the collector plate 16 as shown in FIG. 6. For the vacuum technique, the annular gasket 15 shown in FIG. 1 is placed between the column manifold 14 and the collector plate 16 to provide a relatively air-tight seal."

This passage is directed to an embodiment that employs the vacuum technique. The Examiner has agreed that *Franciskovich et al.* '899 does not teach that plate member 36 seals each of the openings 70 of the two members in view of the fact that the vacuum is simultaneously applied to all ends. The subject passage communicates that when using a gasket a relatively air-tight seal is formed by the gasket between an upper annular edge of collector plate 16 and the lower annular surface of column manifold 14. Column 5, at lines 63-65 states that this gasket 15 is ***not*** required when a centrifuge is employed to drive the sample through the chromatographic separation

medium. This passage taken with the foregoing passage, implicitly teaches that since the gasket 15 is not required when employing a centrifuge, a seal is not formed. Further, it is noted that assuming *arguendo* a seal were to be formed, the seal would be ***only*** between the lower annular surface 23 of column manifold 14 and upper annular surface of collector plate 16. ***Franciskovich et al. never teaches individually sealing each of openings 70 with collector plate 16.***

The Examiner also points to column 5, line 65 to column 6, line 4 of *Franciskovich et al.*, which discusses gasket 15, and is not relevant to the embodiment utilizing a centrifuge. Again, the Examiner has agreed that *Franciskovich et al.* '899 does not teach that plate member 16 seals each of the openings 70 of the two members in view of the fact that the vacuum is simultaneously applied to all ends. The noted passage discusses that to create an air pressure differential within the apparatus, the lower major surface 23 of the column manifold plate 14 serves as a sealing surface against which the gasket 15 butts and that the gasket 15 fits within flange 28 which extends around the column manifold 14. Col. 6 describes that, when in place, the central opening of gasket 15 creates a space between the column manifold 14 and the collector plate 16 which enables all of the wells to be evacuated. This passage teaches that when a gasket is used, openings 70 ***cannot*** be individually sealed. *Franciskovich et al.* never teaches providing a sealing device that individually seals each of openings 70, particularly where the device comprises a tray that comprises a plurality of recesses. *Franciskovich et al.* does not teach individually sealing openings 70 during fluid processing, and in fact requires that openings 70 be open and in fluid communication with wells 34 during fluid processing. *Franciskovich et al.* does not teach during centrifugal processing, sealing column manifold 14 to collector plate 16. *Franciskovich et al.* does not teach individually sealing opening 70 when employing a vacuum processing procedure using gasket 15. None of claims 1-18 of *Franciskovich et al* recite any of the terms "seal," "seals," "sealingly," or "sealing."

In conclusion, *Franciskovich et al.* fails to teach or suggest a sealing device having a surface adapted to individually seal each of the first end openings of a plurality of devices where the sealing device comprises a tray and the tray comprises a plurality of recesses. In fact, *Franciskovich et al.* does not teach a sealing device that seals each of the openings 70, let alone a sealing device that **individually seals** each of the openings 70, or let alone a sealing device that individually seals each of the openings 70 and comprises a tray that comprises a plurality of recesses.

In view of the remarks set forth herein, it is submitted that *Franciskovich et al.* does not teach each and every element of the invention as claimed in claim 1, as required for anticipation under 35 U.S.C. § 102(b). Thus, it is respectfully submitted that claims 1-5, 16, and 19 are novel within the meaning of 35 U.S.C. § 102(b) in view of U.S. Patent No. 5,603,899 to *Franciskovich et al.* Favorable consideration and withdrawal of the rejection are respectfully requested.

(b) Claims 1-9 and 16-19 are patentable over Franciskovich et al. in view of Sanadi.

Claims 1-9 and 16-19 were rejected under 35 U.S.C. § 103(a) as being unpatentable over *Franciskovich et al.* in view of *Sanadi.*

In the Final Office Action, the Examiner, at page 4, item 8, asserts with respect to claim 1, that *Franciskovich et al.* fails to disclose the use of a sealing device having a surface adapted to individually seal each of the first end openings wherein the sealing device is a tray with a plurality of recesses. The Examiner concludes that it would have been obvious to the skilled artisan to provide a sealing device as suggested by the reference of *Sanadi* for the known and expected result of providing means recognized in the art for sealing an array of openings and that use of the device of *Sanadi* would be advantageous because it would eliminate the need for an individual cap for each opening while providing the sealing suggested by the primary reference to *Franciskovich et al.* The Examiner points to column 1, lines 34-64 of *Sanadi.*

It is submitted that *prima facia* obviousness has not been established because:

(i) the combination of *Franciskovich et al.* with *Sanadi* is improper;

(ii) there is no motivation to modify the device of *Franciskovich et al.* by incorporating the sealing tray of *Sanadi*; and

(iii) assuming *arguendo* such motivation to modify exists, the modification would render *Franciskovich et al.* unsatisfactory for its intended purpose, as well as change the principal operation of *Franciskovich et al.* Further, the modification would not achieve a sealing device having a surface adapted to individually seal each of the first end openings of the plurality of devices during processing of the plurality of fluid samples, the sealing device comprising a tray and the tray comprising a plurality of recesses. A brief outline of relevant authority is set forth below.

Regarding motivation to combine references, MPEP 2143 discusses the requirements of a *prima facie* case of obviousness. First, there must be some suggestion or motivation to combine the reference teachings or to modify the reference, and second, there must be a reasonable expectation of success. Finally, the prior art reference or references when properly combined, must teach or suggest all the claim limitations.

MPEP 2143.01 states that there are three possible sources for "a motivation" to combine references: the nature of the problem being solved; the teachings of the prior art; and the knowledge of one of ordinary skill in the art. Further, MPEP 2145(X)(D)(2) states that "It is improper to combine references where the references *teach away* from there combination."

Regarding motivation to modify properly combined references, MPEP 2143 states that where the prior art conflicts, all teachings must be considered and that the fact that references can be combined or modified is not sufficient to establish *prima facie* obviousness. MPEP 2143 further states that there must be some suggestion or motivation to modify the references, and there must be a reasonable expectation of success. In addition, the prior art reference or references when properly combined, must teach or suggest all the claim limitations.

MPEP 2143.01 states that a proposed modification cannot render the prior art unsatisfactory for its intended purpose. If it does, then there is no suggestion or motivation to make the proposed modification. Further, the proposed modification cannot change the principle operation of a reference.

With regard to *teaching away*, MPEP 2141.02 states that prior art must be considered in its entirety, including disclosures that *teach away* from the claims. See also MPEP 2145(X)(D).

The court in *In re Gurley,* 27 F.3d 551 (Fed. Cir. 1994), held that "A prior art reference may be said to 'teach away' when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." The court in *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.,* 796 F.2d 443 (Fed. Cir. 1986), held that "A reference should be considered as a whole, and portions arguing against or teaching away from the claimed invention must be considered."

(i) The combination of *Franciskovich et al.* with *Sanadi* is improper:

It is submitted that the combination of *Franciskovich et al.* with *Sanadi,* is improper because there is no motivation or suggestion supporting the combination. Contrary to the Examiner's assertion that *Franciskovich et al* suggests "...providing the sealing...," and as discussed above, *Franciskovich et al.* does not teach or suggest sealing each of openings 70 or a sealing device that seals each of the openings 70, let alone individually sealing each of openings 70 or a sealing device that individually seals each of the openings 70. In fact, *Franciskovich et al.* ***requires*** that first end opening 70 remain open during processing and, ***requires*** a device 12 that has a first end opening 70 and a second end opening. *Franciskovich et al.* ***requires*** open end 70 in order to process a sample and collect a separated constituent of the sample in a collection well separate from the column 12. Accordingly, *Franciskovich et al.* provides ***no motivation*** to look to art concerned with sealing devices, i.e., *Sanadi.* In fact, *Franciskovich et al.* ***teaches away*** from a combination with *Sanadi* because *Sanadi* ***requires*** a plurality of closed-ended wells or tubes where each well or tube has one closed end and one open end. *Sanadi* ***requires*** processing in the closed-ended well or tube array. *Franciskovich et al.* requires driving a sample through separation column and opening 70, and collecting a separated constituent from a corresponding well 34 of a separate collector plate 16. Accordingly, *Franciskovich et al.* ***teaches away*** from any processing apparatus that does not comprise a first open end and a second open end. Likewise, *Sanadi* requires a tube or a well having one closed end and one open end. Accordingly, *Sanadi* ***teaches away*** from a device having a first open end and a second open end. Further, the skilled artisan given *Franciskovich et al.* and concerned with providing a separation column for processing and having first and second open ends, would have no motivation to look to art requiring a closed end tube, i.e., *Sanadi.* Likewise, the skilled artisan given *Sanadi* and concerned with providing a closed end tube or well for processing, would have no motivation to look to art requiring a separation column having a first and a second open end, i.e., *Franciskovich et al.*

In view of the foregoing, it is submitted that a *prima facia* case of obviousness has not been established because the combination of *Franciskovich et al.* with *Sanadi* is improper.

(ii) Assuming *arguendo* the combination of *Franciskovich et al.* with *Sanadi* proper, it is submitted that the skilled artisan would have no motivation to modify *Franciskovich et al.* in view of *Sanadi*, in order to obtain the present invention.

Franciskovich et al. ***requires*** a separation column having a first open end and a second open end in order to process a sample. Accordingly, the skilled artisan would have no motivation to modify the device of *Franciskovich et al.* by providing a sealing lid as allegedly taught by *Sanadi.*

Franciskovich et al. requires that opening 70 remain opening during processing such that material can flow through opening 70 and be collected into well 34 of a collector device. Accordingly, *Franciskovich et al.* ***teaches away*** from sealing open ends 70, thus, the combination of the sealing lid of *Sanadi* illustrated in Fig. 48 with the manifold and columns of *Franciskovich et al.* to seal openings 70 during fluid processing would: (1) destroy the intent of *Franciskovich et al.*; (2) change the principal operation of *Franciskovich et al.*; and (3) render *Franciskovich et al.* inoperable. *See* MPEP 2143.01 which states that if a proposed modification renders the prior art unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. In addition, there is no motivation to modify *Franciskovich et al.* in view of *Sanadi,* because *Sanadi* also fails to teach or suggest a sealing device having a surface adapted to individually seal each of the first end openings of the plurality of devices during processing of the plurality of fluid samples, the sealing device comprising a tray and the tray comprising a plurality of recesses. In fact, *Sanadi* ***teaches away*** from such a sealing device. *See In re Gurley,* 27 F.3d 551 (Fed. Cir. 1994).

The Examiner points to Fig. 4A of *Sanadi* as disclosing a sealing device or tray 61 with recesses 71. The Examiner points to column 1, lines 34-64 of *Sanadi* as disclosing a variety of well-known means for sealing the openings of an array of openings of an array of tubes.

The embodiment illustrated in Fig. 4 of *Sanadi* is described at col. 8, line 30 to col. 9, line 26. At col. 8, lines 37-46, *Sanadi* recites:

> "Wells **64** have openings whose tops **69** are preferably raised above principal surface **70** of plate **62** making contact with the lower surface **71** of lid **65** when lid **65** is placed in proper alignment on plate **62**. After placing lid **65** on plate **62**, clip **72**, shown here as a flat, flexible friction fit clip, is put into place such that lid **65** is held in plate **62** with downward pressure being exerted by lower surface **71** of lid **65** on raised rims **69** of well **64**. An effective seal would thus be formed by the mating of raised rim **69** and the lower principal surface **71** of lid **65**."

This passage clearly communicates that a "seal" is formed only ***after sufficient downward pressure is exerted*** by lower surface 71 on raised rims 69 via engagement of the flexible, friction fit clip 72. *Sanadi* describes at col. 8, lines 49-53 referring to Fig. 4A, that the annular collars 73 that form the recesses in the lower surface 71 of the lid 65 have an inner diameter that is "...slightly greater than..." an outer diameter of raised rims 69. This passage further supports that lid 65 does not seal wells 64 in the absence of sufficient pressure because a frictional fit between a raised rim 69 and an annular collar 73 is ***impossible*** when an annular collar 73 has an inner diameter greater than an outer diameter of a raised rim 69. Accordingly, lid 65 does not meet the present limitation of "...a sealing device having a surface adapted to individually seal each of ...openings... during processing....", because it is not the surface 71 of lid 65 that individually seals wells 64; rather, it is sufficient downward pressure that seals wells 64.

In further support of the above, col. 3, lines 4-7, of *Sanadi*, referring to an embodiment where a gasket is disposed between a lid and a plate, recites that: "The lid is then clamped ...to the plate...with sufficient force to ...provide sealing contact between the gasket and the ...plate to seal the well openings." *Sanadi* at col. 3, lines 43-45, states that: "...multiple sample containers can be sealed without the use of tight fitting caps or a gasket." *See* also col. 6, lines 18-24, and col. 6, line 60 to col. 7, line 5. *Sanadi* at col. 7, lines 48-50, states: "...of lid **48** is then lowered into place and clamp **50** is put in place in notch **55** of plate **42** thereby sealing the well openings." *See* also *Sanadi* at col. 8, lines 22-26, and col. 10, lines 1-5 and 65-67.

Sanadi ***teaches away*** from "...a sealing device having a surface adapted to individually seal each of ...openings... during processing...." because *Sanadi* teaches that the use of such sealing devices results in cross-contamination between wells when such sealing devices are opened. *Sanadi* describes that prior art sealing devices are undesirable because they result in cross contamination. At col. 1, lines 49-64, *Sanadi*, referring to prior art sealing devices, states:

> "Tapes which are used currently to seal the tops of wells are not very reliable. Adhesive tapes limit the number of conditions that the plate can be subjected to...and heat sealing tape requires specialized.... This problem of cross-contamination is particularly acute when tight fitting caps and tape are opened, which frequently results in aerosol formation. These aerosols...."

Sanadi asserts at col. 2, lines 34-36, that it is an object of the invention to have a tube array that can be sealed ***without*** the use of tight-fit caps. *Sanadi* asserts at col. 3, lines 46-47, that a glass slide is provided that can be sealed ***without*** the use of adhesives. *Sanadi* asserts at col. 5, lines 25 and 33-34, that a sealing layer or gasket should not adhere to principal surface 21 of tray 3 or to lid 1. At col. 6, lines 22-23, *Sanadi* recites that sealing via sufficient downward pressure, upon release of pressure allows opening of the seal without the formation of aerosols which are formed upon opening of tight fitting snap-type caps or adhesive tapes. Thus, *Sanadi* ***teaches away*** from frictional fit and adhesive tape sealing devices.

In view of the foregoing, *Sanadi* does not teach or suggest "...a sealing device having a surface adapted to individually seal each of ...openings... during processing...." and in fact ***teaches away*** from such sealing devices.

In view of the foregoing, it is submitted that a *prima facia* case of obviousness has not been established because there is no motivation to modify *Franciskovich et al.* in view of *Sanadi.*

(iii) Assuming, *arguendo*, that such motivation to modify does exist, the modification would render *Franciskovich et al.* unsatisfactory for its intended purpose, as well as change the principal operation of *Franciskovich et al.* Further, such modification would not achieve the present sealing device of claim 1.

Again, as discussed herein, *Franciskovich et al.* ***teaches away*** from sealing open ends 70, thus, the combination of the sealing lid of *Sanadi* illustrated in Fig. 48 with the manifold and columns of *Franciskovich et al.* to seal openings 70 during fluid processing would destroy the intent of *Franciskovich et al.,* would change the principal operation of *Franciskovich et al.,* and would render *Franciskovich et al.* inoperable. *See* MPEP 2143.01

As discussed herein, both *Franciskovich et al.* and *Sanadi* fail to teach or suggest the present sealing device of claim 1 having a surface adapted to individually seal each of the first end openings of the plurality of devices during processing of the plurality of fluid samples, the sealing device comprising a tray and the tray comprising a plurality of recesses. In fact, both *Franciskovich et al.* and *Sanadi* ***teach away*** from such a sealing device. Please see the discussions set forth herein.

In view of the remarks set forth herein, it is submitted that neither of *Franciskovich et al.* nor *Sanadi*, taken alone or together, render the invention of claims 1-9 and 16-19 obvious within the meaning of 35 U.S.C. § 103(a).

(a) Claims 8 and 9:

Present claim 8 is dependent on claim 1 and present claim 9 is dependent on claim 8. Both of claims 8 and 9 are unobvious over *Franciskovich et al.* in view of *Sanadi*, as discussed herein, and are independently patentable from claim 1, for the following reasons.

Claims 8 and 9 include all of the limitations of independent claim 1 and further recite that the sealing device includes an adhesive (claim 8) and that the adhesive is optically-curable, pressure sensitive, or both (claim 9). The Examiner asserts on page 5 of the Final Office Action, that *Sanadi* describes that the use of a sealing tape is a well known alternative to the use of caps. However, *Sanadi* ***expressly rejects*** the use of adhesives because they cause aerosol formation of sample upon removal, thereby causing cross-contamination. *Sanadi* solves this prior art problem by ***rejecting*** adhesives and providing devices that seal upon application of sufficient pressure. Accordingly, *Sanadi* expressly ***teaches away*** from the invention of claims 8 and 9. The skilled artisan in view of *Sanadi* would not be led to explore adhesive sealing as presently claimed in claims 8 and 9, but would be led in a path divergent from adhesive sealing. *See In re Gurley,* 27 F.3d 551 (Fed. Cir. 1994).

In view of the remarks herein, it is submitted that neither of *Franciskovich et al.* nor *Sanadi*, taken alone or together, render the invention of claims 8-9 obvious within the meaning of 35 U.S.C. § 103(a).

(c) Claims 10, 11, and 13-15 are patentable under 35 U.S.C. § 103(a) over *Franciskovich et al.* in view of U.S. Patent No. 5,846,493 to *Bankier et al.*

Claims 10, 11, and 13-15, were rejected under 35 U.S.C. § 103(a) over *Franciskovich et al.* in view of U.S. Patent No. 5,846,493 to *Bankier et al.*

With regard to claims 10-11, the Examiner asserts that it would have been obvious to the skilled artisan to employ a separation filter as disclosed by *Bankier et al.* in the device of *Franciskovich et al.*

Present claims 10 and 11 are dependent on independent claim 1 and include all of the limitations of independent claim 1. As discussed herein, *Franciskovich et al.* does not teach or suggest the sealing device of present claim 1. Please see the discussions relevant to *Franciskovich et al.* set forth herein. It is submitted that *Bankier et al.* does not cure the deficiencies of *Franciskovich et al.* because *Bankier et al.* also does not teach or suggest the sealing device of present claim 1.

With regard to claims 13-15, the Examiner asserts that it would have been obvious to the skilled artisan to employ any well-known source of nucleic acid based merely on the intended sample to be analyzed. Present claims 13-15 are each dependent on claim 1 and include all of the limitations of independent claim 1. Claims 13-15 each require that the system include a specific biological sample. As discussed herein, *Franciskovich et al.* does not teach or suggest the sealing device of present claim 1. Please see the discussions relevant to *Franciskovich et al.* set forth herein. It is submitted that *Bankier et al.* does not cure the deficiencies of *Franciskovich et al.* because *Bankier et al.* also does not teach or suggest the sealing device of present claim 1.

In view of the remarks herein, it is submitted that neither of *Franciskovich et al.* nor *Bankier et al.*, taken alone or together, render the invention of claims 10-11 and 13-15 obvious within the meaning of 35 U.S.C. § 103(a).

(d) Claim 12 is patentable under 35 U.S.C. § 103(a) over *Franciskovich et al.* in view of *Bankier et al.* taken further in view of U.S. Patent No. 5,955,271 to *Leying et al.* and U.S. Patent No. 5,124,041 to *Sheer et al.*

Claim 12 was rejected under 35 U.S.C. § 103(a) over *Franciskovich et al.* in view of *Bankier et al.* taken further in view of U.S. Patent No. 5,955,271 to *Leying et al.* and U.S. Patent No. 5,124,041 to *Sheer et al.*

The Examiner asserts that it would have been obvious to the skilled artisan to provide the system with PCR reagents for the known and expected result of performing PCR on the purified sample in the filter device.

Present claim 12 is dependent on claim 11 which is, in turn, dependent on claim 1. Accordingly, claim 12 includes all of the limitations of claims 1 and 11. Present claim 12 further

recites that the at least one device includes a polymerase chain reaction solution, a transcription solution, a reverse transcription solution, or a reverse transcription polymerase chain reaction solution. As discussed herein, *Franciskovich et al.* does not teach or suggest the sealing device of present claim 1. Please see the discussions relevant to *Franciskovich et al.* set forth herein. It is submitted that none of *Bankier et al., Leying et al.,* and/or *Sheer et al.* cure the deficiencies of *Franciskovich et al.* because none of *Bankier et al., Leying et al.,* and/or *Sheer et al.,* teach or suggest the sealing device of present claim 1.

In view of the remarks herein, it is submitted that none of *Franciskovich et al.*, *Bankier et al., Leying et al.,* and *Sheer et al.*, taken alone or together, render the invention of claim 12 obvious within the meaning of 35 U.S.C. § 103(a).

(e) Claims 48 and 49 are patentable under 35 U.S.C. § 103(a) over U.S. Patent No. 5,151,719 to *Fernwood et al.* in view of *Sanadi.*

Claims 48-49 were rejected under 35 U.S.C. § 103(a) over *Fernwood et al.* in view of *Sanadi.* The Examiner asserts that it would have been obvious to employ the sealing device of *Sanadi* to seal the openings of the array device of *Fernwood et al.*

Independent claim 48 recites an analytical system that comprises: a plate having a first surface and a second surface that opposes said first surface, and a plurality of through-holes, each through-hole extending from said first surface to said second surface and defining a first end opening at said first surface and a second end opening at said second surface; a plurality of species-immobilizing filters, each disposed within a respective one of said through-holes; and a first sealing device having a surface adapted to individually seal each first end opening of said plurality of through-holes during the manipulation of biological samples, the first sealing device comprising a tray and the tray comprising a plurality of recesses; and a second sealing device adapted to seal each second end opening of said plurality of through-holes. Claim 49 is dependent on claim 48 and recites that the second sealing device comprises a plurality of removable end caps adapted to individually seal the second end openings of the plurality of through-holes.

Fernwood et al. describes in Fig. 4, and at col. 5, a plate assembly comprising an upper plate 11 having a plurality of apertures 12 where a membrane sheet 13 spans the bottom openings

of the plurality of apertures 12 thereby forming sample wells. The upper plate 11 having membrane sheet 13 disposed on a lower surface thereof, is in turn, disposed on a gasket sheet 14 having openings corresponding to the wells. This tri-part structure is then disposed on a drop guide plate 15 having tube passages 41 each of which correspond to a respective sample well, which resultant structure is, in turn, disposed on a support plate 16 which has apertures 18 that permit the tubes of the drop guide plate 15 to pass through into a collection plate 19 disposed below the support plate 16.

Applicants submit that *Fernwood et al.* does not teach or suggest the plate and filters claimed in present claim 48. Present claim 48 recites a plate having a first surface and a second surface that opposes the first surface, and a plurality of through-holes, each through-hole extending from the first surface to the second surface and defining a first end opening at the first surface and a second end opening at the second surface. Applicants are entitled to rely upon the plain meaning of the claim terms "a plate" and "through-hole," as well as the plain meaning of the phrases "each through-hole extending from said first surface to said second surface."

The term "a plate" is both implicitly and explicitly defined in the present specification and is an art-recognized term. Figures 7, 8, and 11, of the present specification, clearly illustrate that the present plate, comprising a plurality of through-holes, is a unitary structure. *See* Figs. 7, 8, and 11 of the present specification and the disclosure related thereto.

In further support of the foregoing, *Fernwood et al.* describes the structure illustrated in Fig. 4, as "a plate assembly" ***not*** a plate. See *Fernwood et al.* at col. 2, line 5. *Fernwood et al.* refers to specific ***elements*** of the plate assembly as "a plate" but ***never*** refers to the plate assembly as a plate. For example, *Fernwood et al.* describes element 11 as "an upper plate 11." See *Fernwood et al.* at col. 2, lines 67-68.

Accordingly, it is submitted that the plate assembly of *Fernwood et al.* does not teach or suggest the "plate" claimed in present claim 48.

Fernwood et al. describes that the openings in the various elements, for example, plates, gaskets and membranes, of the assembly are "aligned" and does ***not*** described the aligned openings as through-holes. *Fernwood et al.* at col. 1, lines 11-13 describe that the narrow tubular passages of the drop guide plate are aligned with the sample wells.

Fernwood et al. states that upper plate 11 contains an array of apertures 12 or ***holes passing completely through*** plate 11. Please see *Fernwood et al.* at the sentence bridging cols. 2 and 3. *Fernwood et al.* states that each tube of the drop guide plate 15 forms a ***through passage*** 41. See col. 4 at lines 28-29. *Fernwood et al.* ***never*** refers to the aligned openings of the plate assembly as "through-holes," "holes passing completely through," or "through passages." *Fernwood et al.* uses these terms ***only*** when referring to an opening traversing a ***single*** element or plate of the plate assembly.

Accordingly, it is submitted that the aligned openings of the plate assembly of *Fernwood et al.* do not teach or suggest the "through-holes" extending from a first surface to a second surface of a plate of present claim 48.

Fernwood et al. describes, at most, that upper plate 11 has a plurality of holes passing completely through upper plate 11, and that the plurality of tubes in drop guide 15 define a plurality of through passages 41. Present claim 48 recites a plurality of species-immobilizing filters, each disposed within a respective one of said through-holes. *Fernwood et al.* does not teach or suggest a species-immobilizing filter ***disposed within a through-hole***. Rather, *Fernwood et al.* describes that a membrane sheet 13 is a continuous uniform sheet that is ***positioned below the wells*** and is sized to span the entire well array, closing off the undersides of each of the apertures 12. See *Fernwood et al.* at col. 3, lines 12-14 and 23-24. Alternatively, *Fernwood et al.* describes, at col. 3, lines 24-26, that individual membrane disks can be ***secured to the bottom of each aperture 12.***

Fernwood et al. does not teach or suggest the presently claimed plurality of membranes each disposed ***in*** a respective through-hole of a plate as claimed in present claim 48. *Sanadi* does not teach or suggest a plate having a plurality of through-holes, or a plurality of membranes each disposed in a respective through-hole of a such plate. Accordingly, *Sanadi* does not cure the deficiencies of *Fernwood et al.*

Present claim 48 recites a first sealing device having a surface adapted to individually seal each first end opening of the plurality of through-holes during the manipulation of biological samples, the first sealing device comprising a tray and the tray comprising a plurality of recesses; and a second sealing device adapted to seal each second end opening of the plurality of through-holes.

Sanadi fails to teach or suggest a sealing device having a surface adapted to individually seal each of the first end openings of the plurality of devices during processing of the plurality of fluid samples, the sealing device comprising a tray and the tray comprising a plurality of recesses. In fact, *Sanadi* ***teaches away*** from such a sealing device. *See In re Gurley,* 27 F.3d 551 (Fed. Cir. 1994). Please see the discussions relevant to *Sanadi* set forth herein.

Further, the combination of the sealing lid of *Sanadi* illustrated in Fig. 4 with the apertures 12 of *Fernwood et al.* to seal the openings during fluid processing would destroy the intent of *Fernwood et al.,* would change the principal operation of *Fernwood et al.,* and would render *Fernwood et al.* inoperable. *See* MPEP 2143.01

As discussed herein, both *Fernwood et al.* and *Sanadi* fail to teach or suggest the present sealing device claimed in claim 48 having a surface adapted to individually seal each of the first end openings of the plurality of devices during processing of the plurality of fluid samples, the sealing device comprising a tray and the tray comprising a plurality of recesses. In fact, both *Fernwood et al.* and *Sanadi* ***teach away*** from such a sealing device. Please see the discussions set forth herein relevant to *Fernwood et al.* and *Sanadi.*

In view of the remarks herein, it is submitted that neither *Fernwood et al.* nor *Sanadi,* taken alone or together, render the invention of claims 48 and 49 obvious within the meaning of 35 U.S.C. § 103(a).

(f) Claims 48 and 49 are patentable under 35 U.S.C. § 103(a) over U.S. Patent No. 5,368,823 to *McGraw et al.* in view of *Sanadi.*

Claims 48 and 49 were rejected under 35 USC § 103(a) over U.S. Patent No. 5,368,823 to *McGraw et al.* in view of *Sanadi.*

The Examiner asserts that it would have been obvious to the skilled artisan to employ the sealing device of *Sanadi* to seal the openings of the device of *Fernwood et al.* It is assumed that the Examiner meant to refer to the device of *McGraw et al.*.

Present claims 48 and 49 are discussed above.

McGraw et al. is directed to a method and apparatus for automated chemical synthesis of oligonucleotides. *McGraw et al.* describes a carrier plate 8 having a plurality of reaction columns

11 formed therein, wherein each of the columns contains a porous support material 7 disposed in the outlet end of the column. The carrier plate 8 is a component of the apparatus. McGraw et al. requires an open inlet end 13 and an open outlet end 14. *See* Figs. 1B and 1C and col. 1, of *McGraw et al.*

It is submitted that *prima facie* obviousness has not been established because:

(i) the combination of *McGraw et al.* with *Sanadi*, is improper;

(ii) assuming, *arguendo*, that the combination is proper, there is no motivation to modify the device of *McGraw et al.* by incorporating the sealing tray of *Sanadi*; and

(iii) assuming, *arguendo*, that such motivation to modify exists, the modification would render *McGraw et al.* unsatisfactory for its intended purpose, as well as change the principal operation of *McGraw et al.* Further, the modification would not achieve a sealing device having a surface adapted to individually seal each of the first end openings of the plurality of devices during processing of the plurality of fluid samples, wherein the sealing device comprises a tray and the tray comprises a plurality of recesses.

It is submitted that the combination of *McGraw et al.* with *Sanadi,* is improper because there is no motivation or suggestion supporting the combination. *McGraw et al.* does not teach or suggest sealing inlet ends 13 or outlet ends 14. *McGraw et al.* does not teach or suggest sealing each of openings 13 or 14 or a sealing device that seals each of the openings 13 or 14, let alone individually sealing each of openings 13 or 14 or a sealing device that individually seals each of the openings 13 or 14. In fact, *McGraw et al.* ***requires*** that the inlet and outlet openings remain open during continuous, automated processing and, ***requires*** that the columns each having an open inlet end and an open outlet end. Accordingly, *McGraw et al.* provides ***no motivation*** to look to art concerned with sealing devices, i.e., *Sanadi.*

In fact, *McGraw et al.* ***teaches away*** from combination with *Sanadi* because *Sanadi* ***requires*** a plurality of closed-ended wells or tubes where each well or tube has one closed end and one open end. *Sanadi* ***requires*** processing in the closed-ended well or tube array. *McGraw et al.* requires an automated continuous process that requires open inlet ends and open outlet ends. Accordingly, *McGraw et al.* ***teaches away*** from any processing apparatus that does not comprise an open inlet end and an open outlet end. Likewise, *Sanadi* requires a tube or a well having one closed

end and one open end. Accordingly, *Sanadi* ***teaches away*** from a device having an open inlet end and an open outlet end, i.e., *McGraw et al.* *See*, M.P.E.P. § 2143.01, MPEP 2141.02, and MPEP 2145(X)(D)(2).

Further, the skilled artisan, given *McGraw et al.* and concerned with providing a column for processing having two open ends, would have no motivation to look to art requiring a closed end tube, i.e., *Sanadi.* Likewise, the skilled artisan, given *Sanadi* and concerned with providing a closed end tube or well for processing, would have no motivation to look to art requiring a column having two open ends, i.e., *McGraw et al.*

In view of the foregoing, it is submitted that a *prima facia* case of obviousness has not been established because the combination of *McGraw et al.* with *Sanadi* is improper.

(ii) Assuming, *arguendo*, that the combination of *McGraw et al.* with *Sanadi* is proper, it is submitted that the skilled artisan would nonetheless have no motivation to modify *McGraw et al.* in view of *Sanadi*, in order to obtain the present invention.

McGraw et al. ***requires*** a column having an open inlet end and an open outlet end in order to automatically and continuously process a sample in the automated apparatus. Accordingly, the skilled artisan would have no motivation to modify the device of *McGraw et al.* by providing a sealing lid as allegedly taught by *Sanadi.*

McGraw et al. ***teaches away*** from sealing open ends 13 and/or 14, thus, the combination of the sealing lid of *Sanadi* illustrated in Fig. 48 with the columns of *McGraw et al.* to seal openings, 13 or 14, during processing, would destroy the intent of *McGraw et al.,* would change the principal operation of *McGraw et al.,* and would render *McGraw et al.* inoperable. *See* MPEP 2143.01 which states that if a proposed modification renders the prior art unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification.

In addition to the foregoing, there is no motivation to modify *McGraw et al.* in view of *Sanadi,* because *Sanadi* also fails to teach or suggest a sealing device having a surface adapted to individually seal each of the first end openings of the plurality of devices during processing of the plurality of fluid samples, wherein the sealing device comprises a tray and the tray comprises a plurality of recesses. In fact, *Sanadi* ***teaches away*** from such a sealing device. *See In re Gurley,* 27 F.3d 551 (Fed. Cir. 1994). Please see the discussions relevant to *Sanadi* set forth herein.

In view of the foregoing, it is submitted that a *prima facie* case of obviousness has not been established because there is no motivation to modify *McGraw et al.* in view of *Sanadi.*

(iii) Assuming, *arguendo*, that such motivation to modify does exist, the modification would render *McGraw et al.* unsatisfactory for its intended purpose, as well as change the principal operation of *McGraw et al.* Further, such modification would not achieve the present sealing device of claim 1.

Again, as discussed herein, *McGraw et al.* ***teaches away*** from sealing the open inlet ends and/or the open outlet ends of the plurality of processing columns. Thus, the combination of the sealing lid of *Sanadi* illustrated in Fig. 4 with the columns of *McGraw et al.* to seal inlet and/or the outlet openings during fluid processing, would destroy the intent of *McGraw et al.,* would change the principal operation of *McGraw et al.,* and would render *McGraw et al.* inoperable. *See* MPEP 2143.01

As discussed herein, both *McGraw et al.* and *Sanadi* fail to teach or suggest the present sealing device comprising a surface adapted to individually seal each of the first end openings of a plurality of devices during processing of a plurality of fluid samples, wherein the sealing device comprises a tray and the tray comprises a plurality of recesses. In fact, both *McGraw et al.* and *Sanadi* ***teach away*** from such a sealing device. Please see the discussions set forth herein.

In view of the remarks set forth herein, it is submitted that neither of *McGraw et al.* nor *Sanadi*, taken alone or together, renders the invention of claims 48-49 obvious within the meaning of 35 U.S.C. § 103(a).

IX. Conclusion

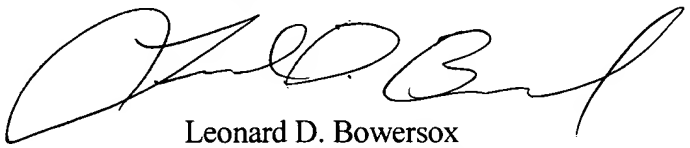
For the reasons discussed in detail above, Appellants submit that: independent claim 1, and dependent claims 2-5, 16, and 19, are novel in view of *Franciskovich et al.;* that independent claim 1 and dependent claims 2-9 and 16-19 are patentable over the combination of *Franciskovich et al.* and *Sanadi;* that dependent claims 10-11 and 13-15 are patentable over the combination of *Franciskovich et al.* and *Bankier et al.*; that dependent claim 12 is patentable over the combination of *Franciskovich et al.* and *Bankier et al.* further in view of *Leying et al.* and *Sheer et al.;* that independent claim 48 and dependent claim 49 are patentable over the combination of *Fernwood et*

al. and *Sanadi;* and that independent claim 48 and dependent claim 49 are patentable over the combination of *McGraw et al.* and *Sanadi*. Accordingly, reversal of the final rejection of claims 1-5, 16, and 19, under 35 USC § 102(b) as anticipated by *Franciskovich et al.,* and reversal of the final rejection of claims 1-19 and 48-49, under 35 USC § 103(a) based on the various combinations of the disclosures of *Franciskovich et al., Sanadi, Bankier et al., Leying et al., Sheer et al., and McGraw et al.,* are respectfully requested.

Should the Board of Patent Appeals and Interferences deem that any further action by Appellants or Appellants' representative is desirable or necessary, the Board of Patent Appeals and Interferences is invited to contact the undersigned at the telephone number set forth below.

Should any additional fees be due in connection with this filing, authorization is hereby given to charge such fees to Deposit Account No. 50-0925.

Respectfully submitted,



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X. Appendix

The Appealed Claims:

Claim 1. A system for processing a plurality of fluid samples, said system comprising:

a plurality of biological sample purification devices, each device of said plurality of devices comprising a tubular body having a first end, a first end opening, a second end, a second end opening, a species-immobilizing filter held within the tubular body, and a removable cap adapted to seal the second end opening; and

a sealing device having a surface adapted to individually seal each of the first end openings of said plurality of devices during the processing of a plurality of fluid samples, the sealing device comprising a tray and the tray comprising a plurality of recesses.

Claim 2. The system of claim 1, wherein the plurality of recesses are formed in said surface, said sealing device is adapted to receive the first ends of said plurality of devices in respective ones of said recesses, and said sealing device is adapted to seal the first end openings of said plurality of devices when the respective first ends of said plurality of devices are received in said recesses.

Claim 3. The system of claim 1, wherein each device of said plurality of devices further includes a second removable cap adapted to seal the first end opening of the respective device.

Claim 4. The system of claim 3, wherein at least one device of said plurality of devices has the respective removable cap attached to the second end of the device and the respective second removable cap attached to the first end of the device.

Claim 5. The system of claim 3, wherein each device of said plurality of devices includes the respective removable cap attached to the second end of the device and the respective second removable cap attached to the first end of the device.

Claim 6. The system of claim 1, wherein said species-immobilizing filter of each device is positioned within the tubular body of the respective device such that the ratio of (1) the distance

from the filter to the first end, to (2) the distance from the filter to the second end, is greater than or equal to about 4:1.

Claim 7. The system of claim 1, wherein said species-immobilizing filter of each device is positioned at the second end of the respective tubular body.

Claim 8. The system of claim 1, wherein the first end opening of each device of said plurality of devices is sealed with said sealing device, and said sealing device includes an adhesive.

Claim 9. The system of claim 8, wherein the adhesive is optically-curable, pressure sensitive, or both.

Claim 10. The system of claim 1, wherein said species-immobilizing filter of each device comprises a nucleic acid purification membrane.

Claim 11. The system of claim 1, further including a target analyte bound to the species-immobilizing filter of at least one device of said plurality of devices, said target analyte comprising a nucleic acid or nucleic acid fragment.

Claim 12. The system of claim 11, wherein said at least one device that includes said target analyte also contains a polymerase chain reaction solution, a transcription solution, a reverse transcription solution, or a reverse transcription polymerase chain reaction solution.

Claim 13. The system of claim 1, further including a biological sample that comprises an animal cell lysate or a plant cell lysate, within the tubular body of at least one device of said plurality of devices.

Claim 14. The system of claim 1, further including a biological sample that comprises whole blood, within the tubular body of at least one device of said plurality of devices.

Claim 15. The system of claim 1, further including a biological sample that comprises tissue extract, within the tubular body of at least one device of said plurality of devices.

Claim 16. A purification apparatus including the system of claim 1, wherein the first end opening of each device of said plurality of devices is sealed by said sealing device in the form of an assembly.

Claim 17. The purification apparatus of claim 16, wherein said assembly further comprises a second sealing device, said second sealing device having a surface adapted to seal the second end openings of said plurality of devices.

Claim 18. The purification apparatus of claim 17, wherein said surface of said second sealing device has a plurality of recesses therein, said second sealing device is adapted to receive the second ends of two or more of said devices in respective ones of said recesses, and said second sealing device is adapted to seal the second end openings of said plurality of devices when the respective second ends of said devices are received in said recesses.

Claim 19. A purification apparatus including the system of claim 2, wherein each device of said plurality of devices is positioned with the respective first end thereof received within a corresponding one of said recesses in said sealing device, in the form of an assembly.

Claim 48. An analytical system for manipulating biological samples, comprising;

a plate having a first surface and a second surface that opposes said first surface, and a plurality of through-holes, each through-hole extending from said first surface to said second surface and defining a first end opening at said first surface and a second end opening at said second surface; a plurality of species-immobilizing filters, each disposed within a respective one of said through-holes; and

a first sealing device having a surface adapted to individually seal each first end opening of said plurality of through-holes during the manipulation of biological samples, the first sealing device comprising a tray and the tray comprising a plurality of recesses; and

a second sealing device adapted to seal each second end opening of said plurality of through-holes.

Claim 49. The system of claim 48, wherein said second sealing device comprises a plurality of removable end caps adapted to individually seal the second end openings of said plurality of through-holes.